Patent
Our Docket: GA0229

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: ROBERTS et al.	)	Art Unit: 1648
Serial No. 09/841,836	)	Examiner: Stacy Brown Chen
Filed: April 4, 2001	)	
For: Preparation and use of particulates composed of adenovirus particles	)	

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Appeal Brief under 37 C.F.R. § 41.37

This Appeal Brief is being filed pursuant to a Notice of Appeal filed on August 17, 2005 in connection with the above referenced patent application. This Appeal Brief was originally due on October 17, 2005. As part of this communication, Applicant is filing a Petition for a Five Month Extension of Time, thereby extending the deadline to file this Appeal Brief to March 17, 2006. Accordingly, this response is timely filed.

TABLE OF CONTENTS:

A. REAL PARTY IN INTEREST

The real party in interest is Genzyme Corporation, the assignee of record.

B. RELATED APPEALS AND INTERFERENCES

There are no related appeal and interferences known to Appellants, which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

C. STATUS OF CLAIMS

Claims 1-20 are currently pending.

Claims 7-20 stand withdrawn from consideration as being drawn to a non-elected invention.

Claims 1-6 stand finally rejected, said rejections are those currently under appeal.

D. STATUS OF AMENDMENTS

No amendments were filed subsequent to the final rejection of the instant claims.

E. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention seeks to enhance the efficiency of adenovirus-mediated gene transfer to dendritic cells by capitalizing on the dendritic cell's ability to engage in endocytosis[1]. To achieve this, the present invention provides adenovirus particulates comprising a plurality of adenovirus particles complexed to an insoluble micro-platform material[2]. These adenovirus particulates provide physical

[1] See, for example, the instant specification at page 3, lines 1-9.
[2] See, for example, the instant specification at page 3, lines 16-20 and page 7, line 30 - page 8, line 2.

properties useful to facilitate the absorption and processing of the particulates by phagocytic antigen presenting cells such as dendritic cells[3].

Claim 1 is drawn to an adenovirus particulate comprising a plurality of adenovirus particles complexed to an insoluble micro-platform material[4]. The adenovirus particles are individual adenovirus virions comprised of an external capsid, which is comprised of adenovirus envelope proteins, and internal nucleic acid material[5]. The micro-platform material refers to a solid, insoluble substance. It comprises a particle of suitable dimensions so that it may be engulfed by a phagocytic cell, such as a dendritic cell[6]. In an embodiment represented by claim 5, the micro-platform is a polymeric fiber or microbead[7]. In an embodiment represented by claim 6, the adenovirus particulate may further comprise a gene encoding an antigenic peptide. The particulate itself may comprise the polynucleotide[8] or the internal nucleic acid of an individual adenovirus virion within the particulate may comprise a gene encoding for an antigenic peptide[9].

Claims 2-4 are drawn to an adenovirus particulate that further comprises a cell-binding ligand that is complexed to the micro-platform material[10]. Claim 2 is broadly drawn to this embodiment. Claim 3 specifies that the cell-binding ligand is specific for a receptor on a dendritic cell[11]. Claim 4 specifies several polypeptide ligands appropriate for dendritic cell receptors, such as GM-CSF, mannose, and mannose-6-phosphate[12].

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[3] See, for example, the instant specification at page 16, lines 4-22.
[4] See, for example, the instant specification at page 3, lines 16-20 and page 7, line 30 - page 8, line 2.
[5] See, for example, the instant specification at page 8, lines 3-6.
[6] See, for example, the instant specification at page 8, lines 7-13.
[7] See, for example, the instant specification at page 17, lines 10-22.
[8] See, for example, the instant specification at page 17, lines 23-26.
[9] See, for example, the instant specification at page 18, lines 5-9.
[10] See, for example, the instant specification at page 16, line 28 - page 17, line 1 and page 19, lines 10-14.
[11] See, for example, the instant specification at page 17, lines 2-9 and page 19, lines 10-14.
[12] See, for example, the instant specification at page 19, lines 10-14.

F. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Whether claims 1, 5, and 6 are unpatentable under 35 U.S.C. §102(e) as anticipated by Blaschuk et al. (U.S. Patent Serial No. 6,358,920)?

2. Whether claims 2-4 are unpatentable under 35 U.S.C. §103(a) over Mountz et al. (WO 98/52615) in view of Blaschuk et al. (U.S. Patent Serial No. 6,358,920) and Lisziewicz et al. (U.S. Patent Serial No. 6,420,176)?

G. ARGUMENT

Errors in the Rejection under 35 U.S.C. 102(e) of claims 1, 5, and 6 as anticipated by Blaschuk et al. (U.S. Patent Serial No. 6,358,920).

1. Brief summary of the applied reference

Blaschuk et al. (U.S. Patent Serial No. 6,358,920); hereinafter referred to as "Blaschuk"

Blaschuk identifies compounds and methods for modulating nonclassical cadherin-mediated functions. Cadherins are a large family of calcium-dependent cell adhesion molecules. There are subclasses within this large family that are grouped by Blaschuk as 1) classical and 2) non-classical. According to Blaschuk, the non-classical cadherin functions were poorly understood. Blaschuk therefore identifies sequences involved in modulating nonclassical cadherin-mediated functions and methods for modulating such nonclassical cadherin-mediated functions as well. In one embodiment, agents useful for modulating these nonclassical cadherin-mediated functions may be polynucleotides. These polynucleotides are formulated to permit expression of a polypeptide modulating agent following administration.

2. Claims 1, 5, and 6 are not anticipated by Blaschuk. Anticipation requires the presence of each and every element of the claimed invention. These elements must not only be present in the cited reference, but they must also be arranged as in the claims at issue. Blaschuk does not disclose the instantly claimed adenovirus particulates which comprise a plurality of adenovirus particles complexed to an insoluble micro-platform material. Hence, no *prima facie* case of anticipation has been or can be established by the Office with the cited Blaschuk reference.

Claims 1, 5, and 6 stand finally rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Blaschuk *et al.*, U.S. Patent No. 6,358,920, referred to hereinafter as Blaschuk. Appellants respectfully traverse.

A claim is only anticipated where the cited prior art reference teaches each and every element of the claim within the prior art reference[13]. Even when the individual claim elements may be present in the prior art reference, anticipation further requires that these elements are arranged as in the claim under examination[14]. Appellants assert that the Office has erred in rejecting the instant claims by not adhering to these basic tenets in the application of 35 U.S.C. 102. The Office has not identified the instant invention in the Blaschuk reference, namely an adenovirus particle complexed to an insoluble micro-platform material.

The Office has concluded that Blaschuk anticipated the instant claims based on the following reasoning. First, the Office has properly concluded that Blaschuk teaches that polynucleotides may function as modulating agents[15]. Second, the Office has also properly concluded that these modulating agents may be linked to a support molecule or a solid support[16]. It is the next step in the Office's logic where Appellants assert the Office has not adhered to the basic tenets for the application of 35 U.S.C. 102. This is because Blaschuk does not teach or suggest that modulating agents include polynucleotides incorporated into vectors. The Office concludes that polynucleotides incorporated into vectors "would still be considered modulating agents and whatever uses described for the modulating agent as a

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[13] Verdegal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."
[14] Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co., 730 F.2d 1452, 1458. "Anticipation requires the presence in a single prior art reference disclosure
[15] See the Office Action mailed February 23, 2005 at page 3, lines 4-5.
[16] See the Office Action mailed February 23, 2005 at page 3, lines 5-6.

polynucleotide would convey to the modulating agent as a vector." The Office further concludes that "One would recognize from Blaschuk's teachings that the polynucleotides or vectors containing them may be linked to a support molecule or solid support..."

Appellants assert that the Office has misconstrued the Blaschuk reference with respect to its application under 35 U.S.C. § 102(e). For the Blaschuk reference to anticipate the instant invention, it must teach an adenovirus particulate. This is an adenovirus particle complexed to an insoluble micro-platform material. Rather than finding the instantly claimed adenovirus particulate, the Office has merely found two elements of the instant invention. The Office identifies in Blaschuk 1) adenovirus particles, which are taught as a polynucleotide delivery means, and 2) a micro-platform material taught as a linker for modulating agents described therein. However, these elements are not arranged as in the instant claims. The Office, not Blaschuk, has combined the two elements by attributing a meaning to "modulating agents" not provided by the Blaschuk reference itself.

As discussed *supra*, Blaschuk is directed to the identification of compounds and methods for modulating nonclassical cadherin-mediated functions. It provides modulating agents capable of modulating one or more functions mediated by a nonclassical cadherin. Blaschuk specifically defines these modulating agents as a molecule comprising at least one of the following four components: 1) a linear or cyclic peptide of specific sequence; 2) a mimetic (peptidomimetic or small molecule) of specific sequence; 3) a substance that binds a peptide of specific sequence; and, most relevant to the instant rejection, 4) a polynucleotide encoding a polypeptide comprising a linear or cyclic peptide of specific sequence[17]. Notably absent from Blaschuk's specific list of modulating agents are polynucleotides incorporated into vectors.

The Blaschuk reference does teach polynucleotides incorporated into vectors, not as modulating agents themselves, but as a means to permit expression of the polynucleotide in a mammal. Appellants

[17] See Blaschuk at column 17, lines 35-51.

reproduce the relevant passage demonstrating this, which is the passage cited by the Office in making the anticipation rejection, here in its entirety:

> As noted above, polynucleotides may also function as modulating agents. In general, such polynucleotides should be formulated to permit expression of a polypeptide modulating agent following administration into a mammal. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a mammal, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector, such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transfected cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art. Other formulations for polynucleotides for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (i.e., an artificial membrane vesicle). The preparation and use of such systems is well known in the art. (See Blaschuk at column 68, lines 10-37.)

Appellants assert that it is evident from a close reading of the above passage that Blaschuk's teachings do not support the conclusion that polynucleotides incorporated into vectors "would still be considered modulating agents and whatever uses described for the modulating agent as a polynucleotide would convey to the modulating agent as a vector." Rather, the Blaschuk reference teaches that there are many ways to formulate and deliver polynucleotides that "(t)hose of ordinary skill in the art will appreciate"[18] to mediate their expression in a mammal. These ways include 1) a "viral vector"[19] (such as adenovirus) comprising the polynucleotide and 2) "other formulations for polynucleotides"[20] such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems. The viral vectors and the "other formulations for polynucleotides" are two separate delivery vehicles by which to achieve expression of Blaschuk's polynucleotide in a mammal. The viral vectors and the microspheres or beads are two independent formulation types for the polynucleotide modulating agent, not components to be combined, according to Blaschuk. In fact, the only examples present in the passage cited by the Office that teach the combination of viral vectors with another molecule are those that incorporate genes

[18] Blaschuk at column 68, lines 15-16.

encoding for targeting moieties into a viral vector or that use of antibodies with a viral vector (column 68, 23-30.) Appellants note that, while Blaschuk does teach that viral vectors may be combined with other molecules, the reference is silent with respect to using microspheres or beads in combination with viral vectors despite Blaschuk's express knowledge of such microspheres or beads.

As such, Appellants assert that the Office has erred in rejecting the instant claims based on anticipation by Blaschuk. For the reference to anticipate the instant invention, it must teach an adenovirus particulate, which is an adenovirus particle complexed to an insoluble micro-platform material. Rather than finding the instantly claimed adenovirus particulate, the Office has merely found two elements of the instant invention in a reference which does not arrange said elements as in the instant claims. The Office, not Blaschuk, has combined the two elements in making the anticipation rejection. Therefore, the Office has not and cannot make a prima facie case of anticipation of the instant claims.

Errors in the Rejection under 35 U.S.C. 103(a) of claims 2-4 over Mountz et al. (WO 98/52615) in view of Blaschuk et al. (U.S. Patent Serial No. 6,358,920) and Lisziewicz et al. (U.S. Patent Serial No. 6,420,176).

1. Brief summary of the applied references

i. Blaschuk et al. (U.S. Patent Serial No. 6,358,920); hereinafter referred to as "Blaschuk":

Described *supra*.

ii. Mountz et al. (WO 98/52615); hereinafter referred to as "Mountz":

Mountz is directed to methods and vectors useful for inducing tolerance in a host to a viral gene therapy vector and prolong expression of a transgene in the host. Antigen-presenting cells that express apoptosis inducing ligands and processed viral vector antigens are utilized to induce the apoptosis of T-

[19] Blaschuk at column 68, lines 18-30.
[20] Blaschuk at column 68, lines 30-38.

cells expressing the ligand receptor. Mountz teaches that adenovirus may be targeted to antigen presenting cells via mannose receptors present on said cells.

iii. Lisziewicz et al. (U.S. Patent Serial No. 6,420,176); hereinafter referred to as "Lisziewicz":

Lisziewicz is directed to methods and compositions for the delivery of genetic material into cells. It takes advantage of natural pathways available in cells and animals, such as receptor-mediated endocytosis or phagocytosis. It teaches further that dendritic cells and macrophages may be targeted through certain receptors including transferrin receptors and mannose receptors.

2. Claims 2-4 are unobvious over the disclosures of Mountz et al. (WO 98/52615) in view of Blaschuk et al. (U.S. Patent Serial No. 6,358,920) and Lisziewicz et al. (U.S. Patent Serial No. 6,420,176). The Graham factual inquiries were not correctly applied in the determination of obviousness under 35 U.S.C. § 103. The Office has not provided all claim limitations with the cited references and has not provided a teaching, motivation, or suggestion to combine the cited references. Hence, no *prima facie* case of obviousness has been or can be established by the Office.

Claims 2-4 stand finally rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Mountz et al. (WO 98/52615) in view of Blaschuk et al. (U.S. Patent Serial No. 6,358,920) and Lisziewicz et al. (U.S. Patent Serial No. 6,420,176). Appellant respectfully traverses.

As stated in the MPEP 2141, it is Office policy to follow Graham v. John Deere Co., 383 U.S. 1, (1966) in the determination of obviousness under 35 U.S.C. 103. This requires determining the scope and content of the prior art, the differences between the prior art and the claimed invention, and the level of ordinary skill in the art. Office policy states that the following basic tenets, which follow from Graham, must be applied during the obviousness analysis (MPEP 2141). These tenets were listed by the Federal Circuit in Hodosh v. Block Drug Co., Inc., 229 USPQ 182, (Fed. Cir. 1986) as follows: 1) The claimed invention must be considered as a whole; 2) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and 3) the reasonable expectation of success is the standard against which obviousness is determined not the "ought to be tried" standard.

Appellant asserts that the Office has erred in rejecting the instant claims by not adhering to these basic tenets in the application of 35 U.S.C. 103.

Furthermore, as stated in MPEP 2142, the Office bears the initial, legal burden of establishing a *prima facie* case of obviousness in accordance with the Graham factual inquiries. The establishment of this *prima facie* case requires three basic criteria. MPEP 2142-2143 outlines these criteria, which the Federal Circuit has consistently required in establishing obviousness where references are combined. There 1) must be a teaching, motivation, or suggestion shown by the Examiner to combine the cited references[21]; 2) all claim limitations must be taught or suggested by the references[22]; and 3) there must be a reasonable expectation of success in making the combination of the references[23].

Appellant asserts that the Office has failed to meet its burden in establishing a prima facie case of obviousness. The Office has failed to properly establish all three criteria in the instant rejection. Moreover, Appellant notes that the Federal Circuit has rejected the establishment of a prima facie case of obviousness where even a single criterion was absent[24].

A. The cited references are not combinable even with the benefit of impermissible reliance on the claimed invention because not all elements of the instant invention are taught in the cited references

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[21] *In re* Rouffet, 47 USPQ 2d 1453, 1457-1458 (Fed. Cir. 1998). "...this court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed."

[22] *In re* Gulack, 703 F.2d 1381, 1385 (Fed. Cir. 1983). "The 1952 act legislatively revised that approach through its requirement that the claim be viewed as a whole in determining obviousness. *Graham v. John Deere Co., 383 U.S. 1, 148 U.S.P.Q. (BNA) 459, 15 L. Ed. 2d 545, 86 S. Ct. 684 (1966).* The CCPA has considered all of the limitations of the claims, including the printed matter limitations, in determining whether the invention would have been obvious. See *In re Royka, 490 F.2d 981, 180 U.S.P.Q. (BNA) 580 (CCPA 1974); In re Cavrich, 59 C.C.P.A. 883, 451 F.2d 1091, 172 U.S.P.Q. (BNA) 121 (1971).*

[23] *In re* Vaeck, 947 F.2d 488, 493 (Fed. Cir. 1991). "Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art [**16] that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." (Citations omitted).

[24] *In re* Rouffet, 47 USPQ 2d 1453 at 1458, (Fed. Cir. 1998). "Lacking a motivation to combine references, the Board did not show a proper prima facie case of obviousness."

The references cited by the Office do not teach or suggest all claim limitations of the instant invention. They fail to provide the required adenovirus particulate, which is an adenovirus particle complexed to an insoluble micro-platform material.

The Office relies on Blaschuk to provide the "general principle of delivering polynucleotides via adenoviral vectors attached to beads.[25]" As discussed above, Appellants assert that the Office has erred in rejecting the instant claims based on anticipation by Blaschuk. For the reference to anticipate the instant invention, it must teach an adenovirus particulate, which is an adenovirus particle complexed to an insoluble micro-platform material. Rather than finding the instantly claimed adenovirus particulate, the Office has merely found two elements of the instant invention, which are not arranged as in the instant claims. Therefore, the Office has failed to provide the required adenovirus particulate and cannot make a prima facie case of obviousness for the instant claims.

B. A teaching, motivation, or suggestion has not been demonstrated by the Office to combine the cited references.

Assuming *arguendo* that the Office has met its burden of providing all elements of the instant invention, the Office fails to provide a detailed statement of motivation, which sets forth the requisite basis for combining the references. Moreover, when the cited references are examined more closely, it is readily appreciated that they teach away from the instantly claimed invention.

(1) The required teaching, motivation, or suggestion to combine the cited references has not been identified by the Office.

The Office's rejection is primarily directed at identifying the various elements that the Office concludes may be combined to arrive at the instant invention. The detailed statement of motivation to provide a basis for combining the references is absent. Rather, the instant rejections contains only conclusory statements to address the motivation behind combining the cited references, as cited below:

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> One would have been motivated to attach the complex of Mountz to a bead, as described by Blaschuk, in order to deliver the vector to the dendritic cell. One would have been motivated to attach mannose to the complex in order to ensure that the dendritic cells take up the complex, since dendritic cells are antigen-presenting cells. (See the Office Action mailed June 30, 2004 at p. 4, lines 7-10.)

These statements seem invoke the knowledge of an artisan as the source for a motivation to combine the references. However, it completely lacks the factual evidence necessary to support this contention. The Office's statement itself cannot suffice as evidence[26]. Moreover, the Office fails to identify the specific rationale or principle known by the hypothetical artisan that would have motivated the specific combination suggested by the Office. When the Office relies on the knowledge of a hypothetical artisan in making an obviousness rejection, this specific rationale, principle, or line of reasoning is required[27]. The Office's rejections above clearly lack a specific, motivating rationale or principle. Appellants assert they are non-specific and unsupported. Certainly more is required by the Office.

The cited references themselves demonstrate the lack of adequate motivation for the combination set forth by the Office. Contrary to the Office's conclusion, one of skill in the art would not be motivated to combine the cited references to arrive at the instant invention.

(2) The primary reference teach away from the suggested combinations

Appellants assert that Blaschuk teaches away from the instant invention. The Blaschuk reference teaches that there are many ways to formulate and deliver polynucleotides that "(t)hose of ordinary skill in the art will appreciate"[28] to mediate their expression in a mammal. These ways include 1) a "viral vector"[29] (such as adenovirus) comprising the polynucleotide and 2) "other formulations for

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[26] *In re* Dembiczak, 50 USPQ 2d 1614, 1617 (Fed. Cir. 1999), *abrogated on other grounds.* "Broad conclusory statements regarding the teaching of multiple references, standing alone, are not 'evidence'."

[27] *In re* Rouffet, 47 USPQ 2d 1453 at 1458 (Fed. Cir. 1998). "...must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination" and "...must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."

[28] Blaschuk at column 68, lines 15-16.

[29] Blaschuk at column 68, lines 18-30.

polynucleotides"[30] such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems. The viral vectors and the "other formulations for polynucleotides" are two separate delivery vehicles by which to achieve expression of Blaschuk's polynucleotide in a mammal. The viral vectors and the microspheres or beads are two independent formulation types for the polynucleotide modulating agent, not components to be combined, according to Blaschuk. In fact, the only examples present in the passage cited by the Office that teach the combination of viral vectors with another molecule are those that incorporate genes encoding for targeting moieties into a viral vector or that use of antibodies with a viral vector (column 68, 23-30.) Appellants note that, while Blaschuk does teach that viral vectors may be combined with other molecules, the reference is silent with respect to using microspheres or beads in combination with viral vectors despite Blaschuk's express knowledge of such microspheres or beads.

Therefore, Blaschuk does not teach or suggest that adenoviral vectors may combined with microspheres and beads even though it specifically contemplates combining viral vectors with other molecules. If the reference itself does not contemplate such a thing, Appellants assert that it is improper to charge one of ordinary skill in the art with the motivation to do so.

C. There must be a reasonable expectation of success in making the combination of the references

In establishing a proper prima facie case of obviousness, a reasonable expectation of success in making the combination of the references must exist. Appellants assert that there is no reasonable expectation of success in arriving at the instant invention by combining the cited prior art references. No reasonable expectation of success can exist because the cited references fail to provide all of the elements of the claimed invention.

As presented above, Appellants have demonstrated that the cited prior art does not contain all of the elements of the claimed invention. None of the prior art references, alone or in combination, teaches

[30] Blaschuk at column 68, lines 30-38.

or suggests an adenovirus particulate. Appellant asserts that no reasonable expectation of success in combining the references can exist where the required elements of the instant invention are not all present.

Accordingly, the Office has failed to establish another required element in a proper prima facie case of obviousness. Appellant also notes that this evidence, demonstrating that there was no reasonable expectation of success may support the conclusion of nonobviousness[31].

Appellant asserts that the Office has erred in applying the Graham factual inquiries and has failed to establish a prima facie case of obviousness. The collection of references fails to teach all the essential elements of the instant invention, which would preclude the combination suggested by the Office. The Office has also used impermissible hindsight reconstruction because they have presented no substantiated motivation or suggestion that would lead one to combine the references. One skilled in the art would not have reasonably expected success in arriving at the instant invention by making the combination because their combination could not have resulted in the claimed invention.

[31] *In re* Rinehart, 531 F.2d 1048, (Fed. Cir. 1976).

H. Claims Appendix

1. (Original) An adenovirus particulate comprising a plurality of adenovirus particles complexed to an insoluble micro-platform material.

2. (Original) The adenovirus particulate of claim 1 further comprising a cell binding ligand complexed to the micro-platform material.

3. (Original) The adenovirus particulate of claim 2 wherein the cell binding ligand binds to a receptor on a dendritic cell.

4. (Original) The adenovirus particulate of claim 3 wherein the cell binding ligand is selected from the group consisting of GM-CSF, mannose, and mannose-6-phosphate.

5. (Original) The adenovirus particulate of claim 1 wherein the micro-platform material is a polymeric fiber or microbead.

6. (Original) The adenovirus particulate of claim 5 wherein the adenovirus particulate further comprises a gene encoding an antigenic polypeptide.

7. (Withdrawn) A method of forming a particulate composed of adenovirus particles comprising mixing adenovirus particles with an insoluble micro-platform material so that the adenovirus particles become complexed to the micro-platform material.

8. (Withdrawn) The method of claim 7 where the micro-platform material is a polymeric fiber or microbead.

9. (Withdrawn) The method of claim 7 wherein the adenovirus particles are complexed to the microplatform material by a crosslinking agent.

10. (Withdrawn) The method of claim 8 wherein the adenovirus particles are complexed to the microplatform material by a crosslinking agent.

11. (Withdrawn) The method of claim 9 where the cross-linking substance is a bivalent antibody.

12. (Withdrawn) The method of claim 10 where the cross-linking substance is a bivalent antibody.

13. (Withdrawn) A method of forming a particulate of adenovirus particles where the adenovirus particle further comprises a gene encoding an antigenic polypeptide.

14. (Withdrawn) The method of claim 7 wherein the particulate of adenovirus particles further comprises a ligand that binds to a receptor on a dendritic cell.

15. (Withdrawn) The method of claim 14 wherein the ligand is GM-CSF, mannose, or mannose-6-phosphate.

16. (Withdrawn) The method of claim 13 wherein the particulate of adenovirus particles further comprises a ligand that binds to a receptor on a dendritic cell.

17. (Withdrawn) The method of claim 16 wherein the ligand is GM-CSF, mannose, or mannose-6-phosphate.

18. (Withdrawn) A method of transfecting a dendritic cell comprising contacting a dendritic cell with an adenovirus particulate of claim 1, thereby transfecting the cell.

19. (Withdrawn) A method of vaccinating a subject against a disease comprising administering to the subject an adenovirus particulate of claim 6, thereby vaccinating the subject against a disease.

20. (Withdrawn) A method of claim 19 where the adenovirus particulate vaccine is administered together with an adjuvant.

I. Evidence Appendix

None.

J. Related Proceedings Appendix

None.

K. Conclusion

Authorization is hereby given to charge the amount of the fee set forth in 37 C.F.R. § 41.20(b)(2) as well as the fee for a Five Month Extension of time to Deposit Account No. 07-1074. No additional fee is deemed necessary in connection with the filing of this communication. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 07-1074.

Respectfully submitted,

3/17/2006
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